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A quantitative ultrasound approach to estimate bone fragility: A first comparison with dual X-ray absorptiometry

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ABSTRACT

Aim of this paper was to assess the discrimination power of a novel ultrasound (US) parameter, called the Fragility Score (F.S.), in the early identification of subjects prone to osteoporotic fractures. A total of 102 female patients were recruited: 49 with a recent osteoporotic fracture (“frail” subjects), 53 were controls without fracture history (“non-frail” subjects). All the patients underwent a spinal DXA (dual X-ray absorptiometry) and an abdominal US scan of lumbar vertebrae. Acquired US data were analyzed by a novel algorithm, which calculated the F.S. through spectral and statistical analyses involving both echographic images and corresponding “raw” signals. F.S. showed a good performance in discriminating “frail” from “non-frail” subjects (sensitivity = 76%, specificity = 68%), resulting even slightly more effective than DXA-measured BMD (sensitivity = 73%, specificity = 66%). This methodology has a potential to become an effective tool for the early identification, and timely treatment, of “frail” subjects.

1. Introduction

Osteoporosis is a systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue, causing an increase in bone fragility and fracture risk [1]. Osteoporotic fractures represent a significant social and economic burden: in Europe, almost 3 million of new osteoporotic fractures occur yearly, causing 43,000 deaths and accounting for a direct cost of about 40 billions of euros [2]. The incidence of osteoporosis and related fragility fractures is globally increasing because of progressive population growth and aging. For instance, people older than 65 years are expected to become 20–25% of the total population in 2030, in comparison to 12–17% in 2002 [3,4]. In Europe, osteoporotic fractures accounts for more Disability Adjusted Life Years (DALYs) lost than most common cancers and it is foreseen that, as life expectancy increases for a greater proportion of the world's population, the financial and human costs associated with osteoporotic fractures will multiply exponentially [5].

Furthermore, despite about 30% of osteoporotic hip fractures in Europe and in USA occur in men, osteoporosis is still perceived as a disease typically related to postmenopausal women, while several literature-available papers underline the importance of undergoing fracture risk assessment tests for both men and women aged 40 years or older [6–9]. In fact, recent estimates predicted that about 30% of all Caucasian women aged 50 years or older will experience one or more osteoporotic fracture in their remaining lifetime, as well as 20% of all Caucasian men of the same age [10].

In this context, novel diagnostic approaches are needed and they should be specifically focused on the identification of subjects at high risk of fracture, rather than on the identification of osteoporotic patients [11–13].

Currently, dual X-ray absorptiometry (DXA) is the most widely used method for diagnosing osteoporosis through bone mineral density (BMD) assessments on lumbar spine and/or proximal femur, and these measurements are often considered as a surrogate of bone fragility assessments and used for fracture risk estimation [14]. Unfortunately, DXA cannot be employed for mass screening purposes, mainly because of accessibility issues related to ionizing radiation employment, very long waiting lists, and high equipment costs [15]. Moreover, some investigators have also questioned the intrinsic DXA suitability for osteoporotic fracture risk assessment, since, although BMD is one of the major determi-

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nant of bone strength, considerable overlaps in BMD values have been reported between individuals that develop fractures and those that do not [16].

These reasons led to an increasing interest in the investigation of ultrasound (US) methods for osteoporosis screening and fracture risk assessment purposes, since US approaches have several intrinsic advantages over DXA, including absence of ionizing radiation, portable devices, lower costs, potential capability of estimating the actual bone strength by interacting with bone microarchitecture [17–20]. In particular, several US metrics for osteoporosis assessment have been recently shown to be potentially useful in a clinical context: apparent integrated backscatter (AIB) [21,22], frequency dependent backscatter coefficient (BSC) [23,24], broadband ultrasound backscatter (BUB) [25], osteoporosis score (OS) [17], spectral centroid shift [26], integrated reflection coefficient (IRC) [27], mean of backscatter difference spectrum and slope of backscatter difference spectrum [28].

In a recent conference paper [29], we preliminarily evaluated the performance of a new US parameter, called the Fragility Score (F.S.), in the identification of "frail" subjects (i.e., those having a "frail" skeletal structure, particularly prone to fracture) from an abdominal spinal scan. In the present work, we performed an extended and more accurate clinical validation of the adopted approach on a larger study population, including also younger women aged in 40–50 years in order to specifically address the most recent international recommendations, which indicate to start periodic fracture risk assessments at the age of 40 years independently of any additional risk factor. Full implementation details of the novel proposed algorithm are also reported, together with a more detailed description of the prototypal US device employed for data acquisition and the adopted patient scan procedure.

2. Materials and methods

2.1. Patients

The study was conducted at the Operative Unit of Rheumatology of "Galateo" Hospital (San Cesario di Lecce, Lecce, Italy), where 102 postmenopausal Caucasian female patients [40–80 years; BMI (body mass index) < 30 kg/m^2; medical prescription for a lumbar DXA] were recruited: 49 of them had reported a recent non-vertebral osteoporotic fracture ("frail" subjects), while the remaining 53 were controls without fracture history ("non-frail" subjects).

Data reported in Table 1 shows the absence of significant differences in terms of both age and BMI between the two considered groups, which, therefore, could not be effectively discriminated on the basis of either of these two parameters.

The study included only female patients because the men that are referred for BMD assessments are very low in number (the typical rate is about 1/15 of the corresponding one for women) and, therefore, the achievement of a statistically significant number of men would have required a too long observation period, incompatible with the planned duration of the present study.

All the recruited patients underwent two examinations: a spinal DXA and an abdominal US scan of lumbar spine, as detailed in the next paragraphs. Each participant gave her informed consent.

Table 1
Overall characteristics of the enrolled study population.

Parameter	"Frail" subjects (mean ± SD)	"Non-frail" subjects (mean ± SD)	*p*
Age (years)	63.0 ± 10.2	64.7 ± 8.5	n.s.
BMI (kg/m^2)	24.33 ± 2.40	24.52 ± 2.67	n.s.

2.2. DXA measurements

Spinal DXA scans were performed with hip and knee both at 90° of flexion using a Discovery W scanner (Hologic, Waltham, MA, USA). BMD was measured over the lumbar vertebrae L1–L4, and the mean value was expressed as grams per square centimeter (g/cm^2). BMD computation was performed by using the DXA manufacturer software (QDR System Software, Version 12.6.2).

DXA equipment underwent daily quality controls and regular maintenance for the entire study period.

2.3. US acquisitions

Abdominal US scans of lumbar vertebrae were carried out by employing a 3.5-MHz convex echographic convex probe (C3.5/60/128 Z, Telemed Medical Systems, Milan, Italy) connected to an innovative US device developed in Lecce (Italy) within the ECHOLIGHT Project through a collaboration between CNR-IFC (National Research Council, Institute of Clinical Physiology) and Echolight srl. The echographic device allowed the acquisition of both conventional images and unprocessed radiofrequency (RF) signals, digitized at 40 MegaSamples per second, 16 bits, and transferred via USB to a PC hard-disk for subsequent analyses. A picture of the employed device is reported in Fig. 1, showing the US device (which measures 33 cm in diameter and 10 cm in thickness) mounted on a medical kart equipped with a 19-in. panel PC.

Each patient underwent a sagittal scan of the lumbar spine, with the probe being moved back and forth from L1 to L4 lumbar vertebrae. Scan duration was about 1 min and generated 100 frames of RF data that were acquired and stored in the PC. Scan depth and transducer focus were each time selected in order to keep vertebral interfaces in the US focal region. The other US parameters were the same for all the acquisitions: power = 75%

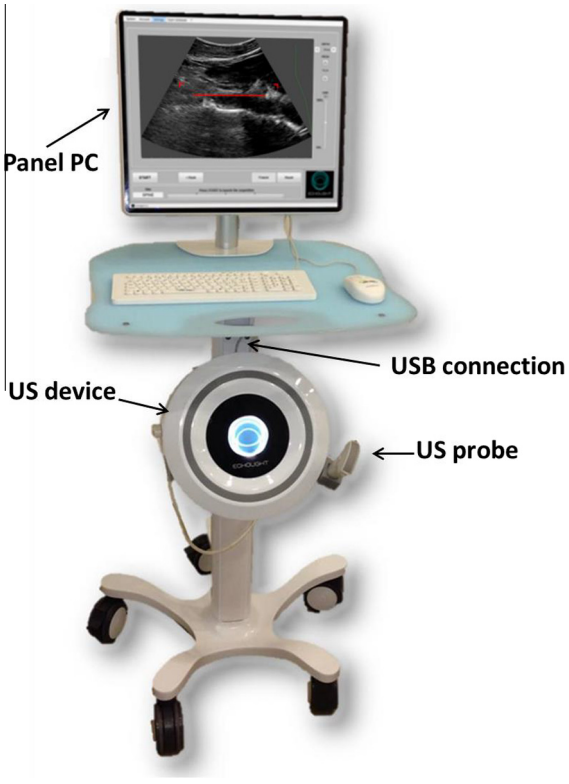

Fig. 1. The employed US device mounted on a medical kart equipped with a 19-in. panel PC. The US device measures 33 cm in diameter and 10 cm in thickness.

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